

SUNSCREENS

Use and Misuse

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Sunscreens are in common use, with more than half of the public buying or using sunscreens within a 3-year period.³² Sun avoidance and regular sunscreen use are widely promoted by organizations and individuals interested in cancer prevention; however, 70% of those who participated in a beach survey were on the beach to get or maintain a suntan.⁵⁷ Although they stayed on the beach for an average of 4 hours, only half were using sunscreen.

There appears to be some confusion in the public health sunscreen message or in the public's interpretation of that message. Some use sunscreens to prevent sunburn, whereas others use sunscreens to improve sun tanning. Some wish to avoid the wrinkling associated with sun exposure, whereas others believe that sunscreens prevent all types of skin cancer. Others seem to believe sunscreens should be used to prolong their time in the sun.

Despite, or conceivably because of, the confusing message, sunscreen use remains sporadic. The majority of male college students in North Carolina "rarely, if ever, use sunscreens."⁵⁰ Fewer than 10% of the students used sunscreens in each instance of intentional sun exposure exceeding 30 minutes. In a study of more than 10,000 subjects, fewer than one third were very likely to use sunscreen, wear protective clothing, or seek shade."²¹ Despite past sunburn experience, skiers often do not use sunscreens. A springtime survey of skiers in Alberta showed that only two thirds were using sunscreen, and of those using a sunscreen, one third were sunburned at the time of survey.²⁸ Even in situations of high sunburn risk, sunscreen use is less than ideal.

Sunscreen use is perhaps most prevalent in Australia where three fourths of adult patients visiting a family physician reported using a sunscreen.³¹ Indeed, sunscreen use was more popular than seeking shade, altering the time of day of exposure, or wearing covering clothing. The reverse priority sequence is commonly recommended by public health authorities.

Childhood exposure to the sun continues to be significant. Past experience of sunburn is a more significant

determinant of childhood sunscreen use than other concerns.⁵⁶ Despite this fact, only one third of U.K. parents regularly protect their children from the midday sun, and approximately half of their children burn at least once a year.⁷ Early childhood exposure continues to be significant, with estimates that children aged 9 to 10 years sustain even more exposure than adolescents aged 14 to 15 years.¹¹

The Application rate

The application rate of sunscreens does not correlate well with the amount used in sunscreen testing. In other words, the average user of sunscreen tends to use significantly less sunscreen than the amount required to achieve the SPF listed on the container

Sunscreen SPF ratings are determined in the United States on the basis of testing at 2 Mg/CM². The rate in Europe is 1.5 Mg/CM². In actual use, it would appear that far less is generally applied. Two studies have suggested that sunscreen use is between 0.5 mg and 1.0 Mg/CM². Thus, sunscreen SPF 15, as it is commonly used, can have a real SPF between 3 and 7.

Despite this known under-utilization of sunscreen, the regulatory authorities have not changed the requirements to coincide with clinical reality. Apparently knowledgeable organizations are still recommending the use of a sunscreen SPF 15 despite the data that a far lower number is the reality in clinical practice. Few, if any, public health messages convey to the public the amount of sunscreen that should be applied.

Many of our recommendations make the statement that frequent application of a sunscreen during the day is required, but there is evidence against this recommendation. A group of children had a split application of an SPF sunscreen followed by unrestricted activity with 6 hours of sun exposure equivalent to 13 times the minimal erythema dose (MED) for these children's skin types.³⁷ One application was made to one side of the body and four applications to the other. One application provided the same level of protection as four applications, confirming the adequacy of a single daily application of a sunscreen in that situation. Sunscreens

are very expensive for some patients, and the requirement for repeated applications may well limit sunscreen use.

It has also been suggested that sunscreens should be applied 30 to 60 minutes prior to going outdoors. As molecules of sunscreen are present in their active state in the sunscreen, sunscreens work immediately upon application. The only reason for application early is to allow absorption so that the sunscreen is less likely to be washed off should the person be entering water. Even then, modern substantive sunscreens are quite resistant to removal from the skin.

Recommendations, if made by physicians, should be evidence-based.

Sun Protective Factor

There is considerable disparity between laboratory SPF and real use SPE. An SPF 6 sunscreen applied to 24 volunteers and tested with an artificial light source according to standard FDA regulations was, of course, a number 6 SPF.³⁶ In sunlight, that same SPF 6 sunscreen had a protective factor of only 4.8. Although testing with artificial light sources is potentially useful for standardization, there have been few studies that directly correlate the results of such standardized testing with results obtained in natural sunshine. It was stated by Sayre et al⁴³ that "a standard product always provided less protection for a natural sunlight spectrum than its label suggests" Public education messages should bear this in mind. The stated SPF is not relevant to assessing the degree of long-wave UVA protection. There are two major types of UV damage: UVC-type damage has a direct effect on DNA, and UVA-type damage has an indirect effect on DNA through other active molecules. UVC, UVB, and short-wavelength UVA (UVA2) up to 340 nm cause UVC-type damage. Light between 340 nm and 400 nm (UVA1) causes UVA-type damage. Sunscreens making claims of UVA protection are legally allowed to do so if they block in the short wavelength UVA range where the UVC type damage is being caused, even though they may have very little effect on UVA1.

UVA would appear to be important to carcinogenesis at least in animal models.¹⁴ Also it is well documented as a significant cause of apparent photoaging.²⁷ Regulators have not yet addressed the issue of a UVA rating for sunscreens. It is very probable, indeed it is intuitively obvious, that a sunscreen that blocks UVB, UVA2, and UVA1 is likely to provide a better protection than one that blocks only UVB and UVA2. Outside of the United

States, there is a good availability of such broad spectrum sunscreens. UVA1 blockers such as Parsol 1789 are much less common in U.S. sunscreens, presumably because of the laborious and expensive FDA approval process.

The active ingredients of transparent sunscreens absorb photons of light and usually release the energy as vibrational energy (heat). It has traditionally been thought that the physical sunscreens reflect light from the surface of the skin back into the environment; however, we now know that there is absorption of microfine titanium to at least the basal layers of the epidermis.⁴⁷ This observation has ramifications to our assessment of the relative safety of transparent versus physical sunscreens. Traditional thought has been that physical sunscreens were safer than transparent sunscreens because all of the energy was reflected from the skin. If the energy is reflected within the epidermis by absorbed titanium dioxide, there could be enhanced, rather than reduced, damage. Further studies are needed.

Sunscreens and the Elderly

Those who treat elderly patients with skin cancers and preskin cancers should be careful to counsel patients in accordance with what is known about carcinogenesis. There appears to be a significant latent period from sun damage to skin cancer development. Certainly, sunburns in childhood appear not to be associated with skin cancers for at least 10 to 15 years, usually longer. In standard carcinogenesis models, initiation is followed by a series of promotional events. More recent sunburn might well be a promotional event, as could non-sun-related inflammatory events. Despite these potentially significant late events, few elderly are likely to develop new skin cancers from present sun exposure. However, after the diagnosis of an actinic keratosis or basal cell carcinoma, many elderly become anxious and almost leap from shadow to shadow. They can become quite obsessed by sun avoidance, and quality of life can be negatively impacted. Ordinary elderly should be counseled to refrain from excessive sun avoidance and enjoy life. The outdoor active elderly should use the prudent approaches recommended for younger adults, mainly to prevent sunburn.

A former concern was that sunscreen use in the elderly might lead to vitamin D deficiency, but it has been laid to rest, to a certain extent. At least, over one summer, an SPF 17 sunscreen did not significantly alter serum vitamin D levels in 113 subjects over age 40.³⁰ Approximately one half of these subjects were older than

70 years of age. As the elderly are known to have an age-related decrease in vitamin D production following equivalent amounts of UV exposure, they may have a higher risk of osteoporosis.²⁹ Some sun exposure in the elderly is probably to be recommended.

Skin Reactions to Sunscreens

Sunscreen can be both an irritant and an allergen. Many patients are convinced that they are allergic to certain active ingredients, although they are not. Allergic reactions are rare.

In an Australian study, 603 subjects used an SPF 15 plus sunscreen versus control, and 19.9% of sunscreen users had an adverse event.¹³ That adverse event was most commonly an irritant reaction. No subject developed an allergic reaction to an active sunscreen ingredient. It would appear that the rate of allergic reaction to sunscreen ingredients is significantly overstated.

Part of our belief in the high allergic potential of sunscreens may have resulted from reports from photomedicine centers. Even in such centers, sunscreen allergies are uncommon. For instance, in one series, 283 patients had photodermatitis; 35 were cases of photoallergy to oxybenzone and 17 to para-aminobenzoic acid.⁴⁶ In another study of 108 patients, there were only four cases of reaction to oxybenzone and four cases of photoallergy to other sunscreen ingredients.⁴⁹

Irritant reactions abound. A classic error in sunscreen application is to put a large amount of sunscreen on the forehead. With perspiration and gravity, the sunscreen migrates down the forehead into the eyes, causing a stinging sensation. Some patients attribute this to an allergic reaction and discontinue sunscreen use. It is prudent to recommend the application of only a modest amount of sunscreen to the forehead and to recommend washing one's hands, if possible, after sunscreen application; rubbing a finger near the eye can induce an irritant reaction if the finger is covered with sunscreen.

Photodegradation

The effect of photodegradation on sunscreen efficacy is not well understood. Sunscreen active ingredients absorb ultraviolet light, sometimes resulting in photodegradation, which can be a major limiting factor to the usefulness of any particular sunscreen ingredient. Photodegradation can be reduced through the addition of stabilizing components. For instance, there is some evidence that the addition of an ingredient, such as Mexoryl SX, (L'Oreal,

Clinchy), can reduce the photodegradation of Parsol 1789 (Givandan-Roure, Clifton). Other factors can also stabilize or enhance sunscreens. These factors include iron chelators⁵ or vitamins C or E.⁹ These factors have a synergistic effect when added to classic sunscreen ingredients, perhaps in part through reduced photodegradation. Additional research as to the effect of photodegradation and its clinical relevance is required.

Why Use Sunscreens?

Reasons for recommending sunscreens to patients should be clear and should be evidence-based. Sunscreens certainly prevent sunburns in many situations, and it is to this burn prevention that the sun protective factor refers. The endpoint of SPF testing is sunburn. Quality of life of those with significant outdoor activities can be improved substantially through the use of high SPF broad spectrum sunscreens to prevent sunburn. The recommendation of sunscreen use to prevent sunburns is well supported by evidence.

There is also substantial animal evidence that high SPF sunscreens with broad spectrum protection can reduce the stigmata of photoaging. UVA-induced sagging of the skin has been reduced in experimental animals by the application of sunscreens. Because UVA penetrates more deeply into the skin than UVB, a significant proportion of chronic photodamage may be secondary to UVA effects.¹⁰

Cancer prevention by sunscreen use is more problematic. Certainly, recent and lifetime sun exposures are risk factors in the development of squamous cell carcinoma in humans.^{15 42} Actinic keratoses have been shown to be preventable by the use of sunscreens.^{35 48} As actinic keratoses are known precursors of squamous cell carcinoma, by inference, the use of sunscreens should prevent squamous cell carcinoma. Supporting this hypothesis is evidence that lip squamous carcinoma is less common in women who use lip protection than in women who do not, or in men.³⁹ Not only do fewer actinic keratoses develop in patients using a high SPF sunscreen but also some pre-existing actinic keratoses can regress. A study in Australia of 558 subjects using SPF 17 sunscreen, compared to vehicle alone, showed that the prevalence of actinic keratoses was significantly reduced in the sunscreen group owing to reduced new lesions and to enhanced disappearance of actinic keratoses.⁴⁸ The sunscreen group showed an actual decrease in pre-existing actinic keratoses of 0.6 per subject over one summer of sunscreen use, versus a mean increase-in

actinic keratoses of 1.0 per subject in the control group. It has been noted by McGregor³² that the "cancer protection-factor" observed in these studies, as manifested by actinic keratosis reduction, is significantly less than the "sunburn protection factor."

Although there is clear evidence that sunscreens are helpful in preventing actinic keratoses and, by inference, squamous cell carcinoma, there is surprisingly little evidence for efficacy in preventing basal cell carcinoma. It may be relevant that there is good epidemiologic evidence to suggest that the pattern of ultraviolet light exposure inducing squamous cell carcinoma is different from that inducing basal cell carcinoma development. Squamous cell carcinoma risk is linked to a cumulative lifetime exposure, with a greatly increased risk at higher exposure levels. Basal cell carcinoma is linked to smaller amounts of UV exposure at an early age.^{15,42} Indeed there may be a slight reduction in risk of basal cell carcinoma at higher recreational exposure levels attained later in life.^{15,42} Sun exposure in childhood and adolescence (age 15 to 19) appears to be a major predictor of basal cell carcinoma risk.^{15,26} Also, whereas sunscreen use in childhood might be presumed to be helpful, there is currently no evidence that sunscreen use prevents basal cell carcinoma development. With the apparently very long latent period from childhood exposure to basal cell carcinoma development in late adulthood, studies to establish such utility of sunscreens are very difficult to perform. That said, the reality is that there is currently no evidence that sunscreen use prevents basal cell carcinoma.

Evidence for the role of sunscreens in the prevention of malignant melanoma is even more problematic. Although there is limited evidence that lentigo maligna melanoma, which most typically appears on areas of maximum sun exposure, follows an etiologic pattern similar to that of actinic keratosis and squamous cell carcinoma, most melanoma does not. There is substantial evidence that melanoma risk rises rapidly with increasing exposure to ultraviolet light in childhood and is somewhat reduced in those individuals maximally exposed to ultraviolet light in the occupational setting as adults.^{12,17} Outdoor workers have a substantially lower risk of melanoma than workers only intermittently exposed to ultraviolet light. Additionally, superficial spreading and nodular melanoma are as common on areas of the skin that are only intermittently exposed (the back of men and women and the lower legs of women) as they are on areas of maximum exposure (the bridge of the nose, malar skin,

backs of the hands, or forearms). Unlike squamous cell carcinoma, the character and timing of solar exposure in patients with melanoma or basal cell carcinoma appear to be more important than the cumulative dose.

There is little direct evidence that sunscreen use prevents melanoma. Indeed, a meta-analysis of papers by Wille et al⁵³ suggested that seven of nine papers showed an odds ratio of greater than 1.0 for sunscreen use linked to melanoma risk. For example, in a recent study, Westerdahl et al⁵² compared 400 melanoma cases with 640 matched controls showing that there was an odds ratio of 1.8 when comparing "almost always" versus "never" using a sunscreen. In other words, they showed an increased risk of melanoma in those using sunscreens. A similar increased risk was shown in a study by Autier et al, 1 in 1995, comparing 418 melanoma patients with 438 controls and showing an odds ratio of 1.5 (95% confidence intervals of 1.0 to 2.06) for the regular use of sunscreens. Although these studies show that an apparently increased risk of melanoma with sunscreen use is of some concern, there are significant difficulties in interpreting the results as showing a positive relationship between sunscreen use and cancer risk. It is acknowledged that some studies may have significant confounders that could have given a false impression. Confounders may also be relevant to the only two studies that have suggested possible benefit.^{24,38} Thus, it would appear to be prudent for our recommendations to take into account the tenuous nature of evidence that sunscreen use prevents melanoma.

Density of acquired melanocytic nevi, whether whole body counts or on a single anatomic site, is the single greatest predictor of melanoma risk.^{18,23} Number of nevi correlates strongly with childhood UV exposure. Although studies of melanoma prevention may be difficult to undertake, studies of preventing the most common precursor of melanoma, and the best documented risk factor of melanoma, may be revealing. Gallagher et al¹⁸ studied a cohort of school children in the Vancouver school system and compared regular sunscreen use to a control group with ambient sunscreen use. They showed a trend to a reduction in number of new nevi in the group receiving regular sunscreens. However, the analysis did not control for all potential confounders. The results are suggestive of a possible benefit of sunscreen use, but further studies are required.

In summary, there is good evidence that appropriate broad spectrum sunscreens can prevent some aspects of

photoaging and can prevent actinic keratosis and, perhaps by inference, squamous cell carcinoma. Sunscreens can prevent sunburn. There is no balance of evidence that would suggest that sunscreens directly prevent basal cell carcinoma or melanoma.

Immunosuppression

Immunosuppression caused by ultraviolet light appears to be a significantly under-appreciated phenomenon. There is growing evidence that such immunosuppression is of biologic significance. Suberythemal doses of UVB can induce immunosuppression.⁵¹ Ultraviolet light can induce cis-urocanic acid in the epidermis, which is a known immunosuppressant.¹⁰ There is also evidence that ultraviolet light can induce interleukin-10, which is also a potent immunosuppressant.

There is evidence that ultraviolet light can suppress resistance to infection. The equivalent of 100 minutes of solar exposure at midday in Italy suppresses resistance to infection with *Listeria monocytogenes* to a medically significant degree.¹⁹ It is not known what role UV exposure has in the propagation of many diseases that are observed in the tropics.

It is clear that sunscreens can reduce immunosuppression, but they do not prevent it.^{11 22 40 54 55} Although it is apparent that both UVA and UVB are potent immunosuppressants, few studies have been done on the visible wavelengths of light.

Even relatively small amounts of UVB in the absence of sunscreen can depress the Langerhans' cell population for more than 2 weeks.³⁴ This prolonged effect may be relevant to more than just cutaneous oncology. Considering that lymphocytes circulate within range of UVA, there may be profound systemic alterations yet to be defined. Non-UV-induced immunosuppression is clearly relevant to the development of skin cancers of various types. In renal transplant patients in Australia, 70% developed squamous cell carcinoma after 20 years of immunosuppression.⁸ There was no link to a specific immunosuppressant agent, suggesting that

immunosuppression from any cause might be relevant to skin cancer development.

An increase in nevus count is clearly related to immunosuppression. Renal transplant patients had significant increases in their nevus counts,⁴⁴ as did children who received chemotherapy for lymphoproliferative disease.³ Number of nevi, as has been previously noted, is the single greatest predictor of melanoma risk. Even in diseases such as xeroderma pigmentosum in which there was a previously understood causation not overtly related to immunosuppression, there now appears to be a significant immune defect in response to UVB.³³ Other syndromes associated with an increased risk of skin cancer may show similar abnormalities.²⁵

Conclusion

The use of sunscreens has been well defined. Broad spectrum sunscreens are very useful in reducing accidental sunburn. There is some evidence that, when avoidance of the sun is impossible, sustained sunscreen use can also reduce the stigmata of photoaging and probably actinic keratoses, and by extension, perhaps squamous cell carcinoma. There is no balance of evidence that sunscreen use prevents melanoma or basal cell carcinoma, although, intuitively, sunscreens consistently used from childhood should reduce risk of these cancers. Our public messages should be clear and should be evidence based. Behavior modification studies are required.⁴¹ Even in Australia, where there has been an intensive educational program, recent sunburn experience prevalence is unchanged.² The public continues to receive, or to assemble for themselves, very mixed messages. For instance, sunscreens were most commonly used by sunbed users in one recent study.⁶

Our recommendations as physicians should be evidence-based and supportable. Collaborative work with regulators is needed to allow the rapid deployment of broad spectrum sunscreens. Research into behavior change should be encouraged, as should research into such issues as photodegradation and immunosuppression. The role of sunscreens in preventing basal cell carcinoma and melanoma remains to be defined.

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